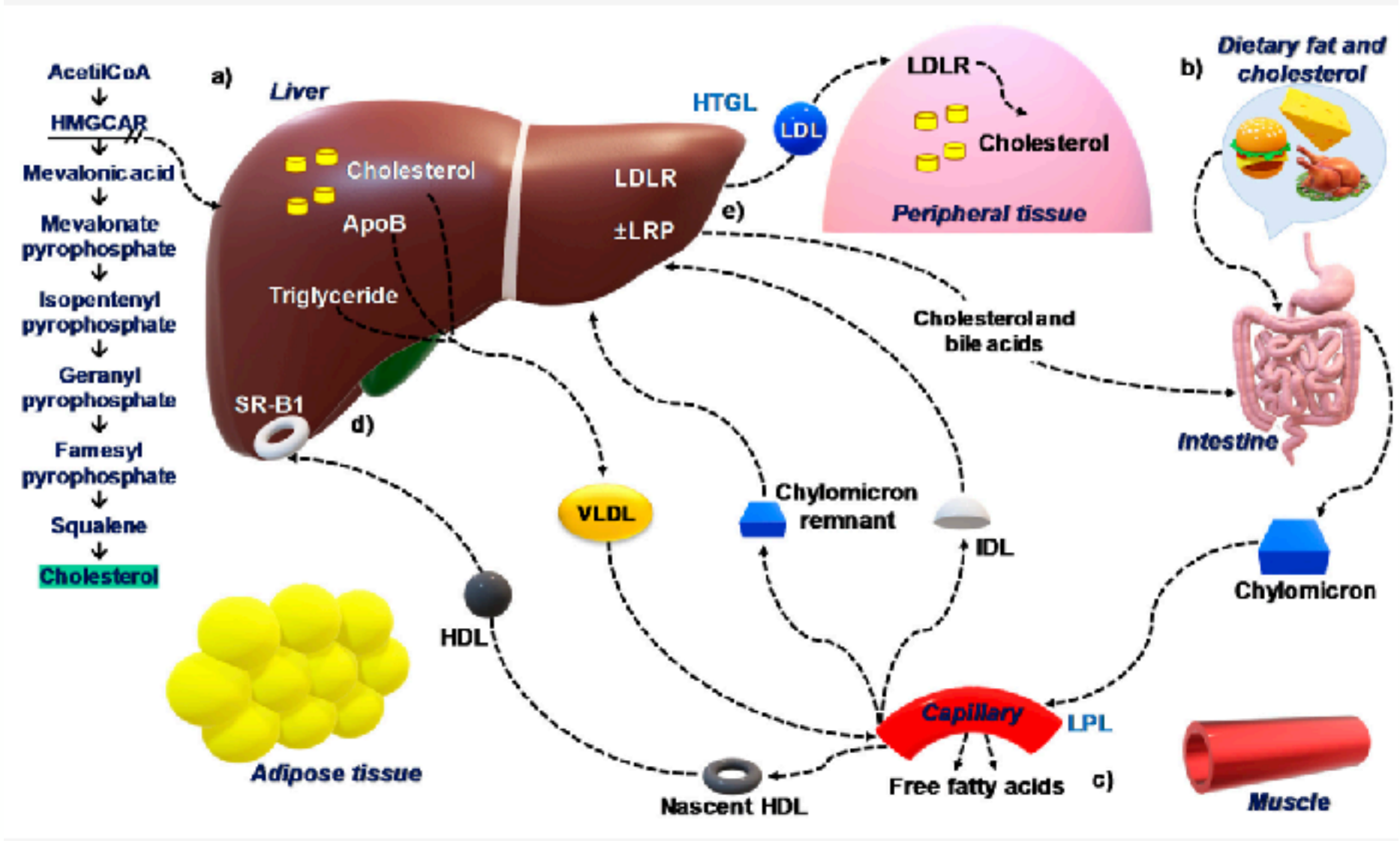
HARTCENTRUM Noord Antwerpen

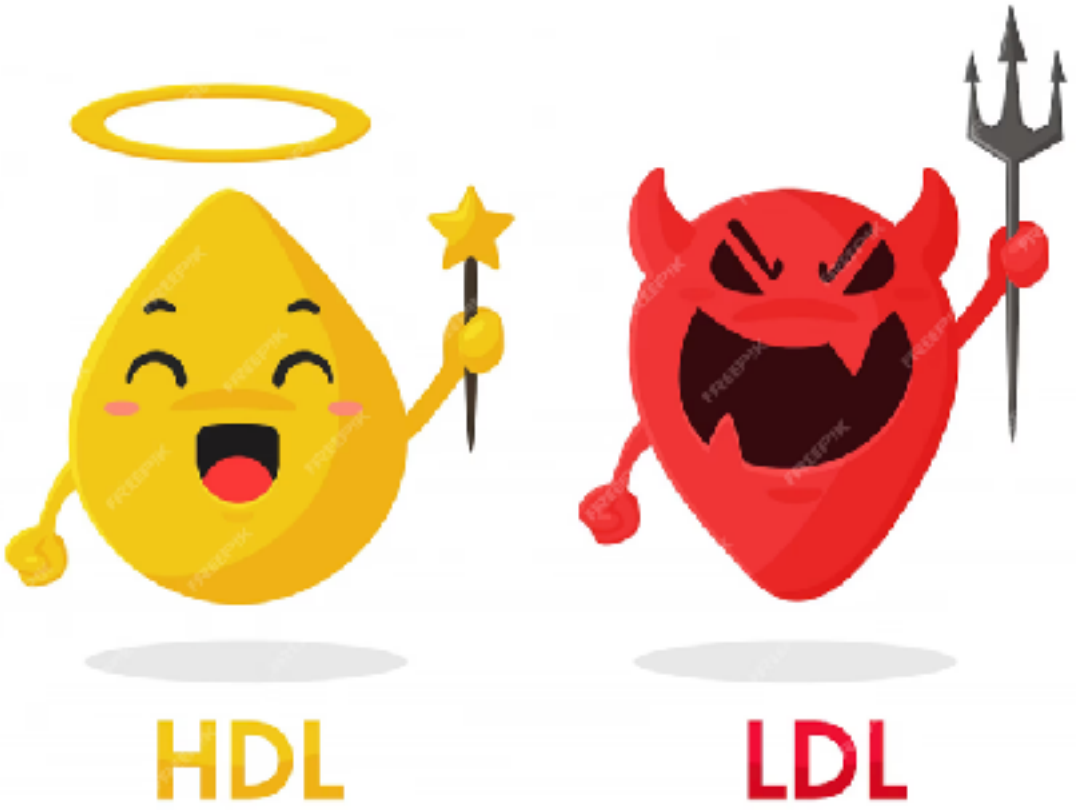
AZ Klina voluit voor zorg

Lipiden

Dr. I. Rooms


AcetilCoA
HMGCAR
Mevalonic acid
Mevalonate pyrophosphate
Isopentenyl pyrophosphate
Geranyl pyrophosphate
Farnesyl pyrophosphate
Squalene
Cholesterol
a)
Liver
Cholesterol
ApoB
Triglyceride
SR-B1
d)
HTGL
LDL
LDLR
±LRP
e)
LDLR
Cholesterol
Peripheral tissue
b)
Dietary fat and cholesterol
Cholesterol and bile acids
Intestine
VLDL
Chylomicron remnant
IDL
Chylomicron
HDL
Capillary
LPL
Free fatty acids
c)
Muscle
Adipose tissue
Nascent HDL

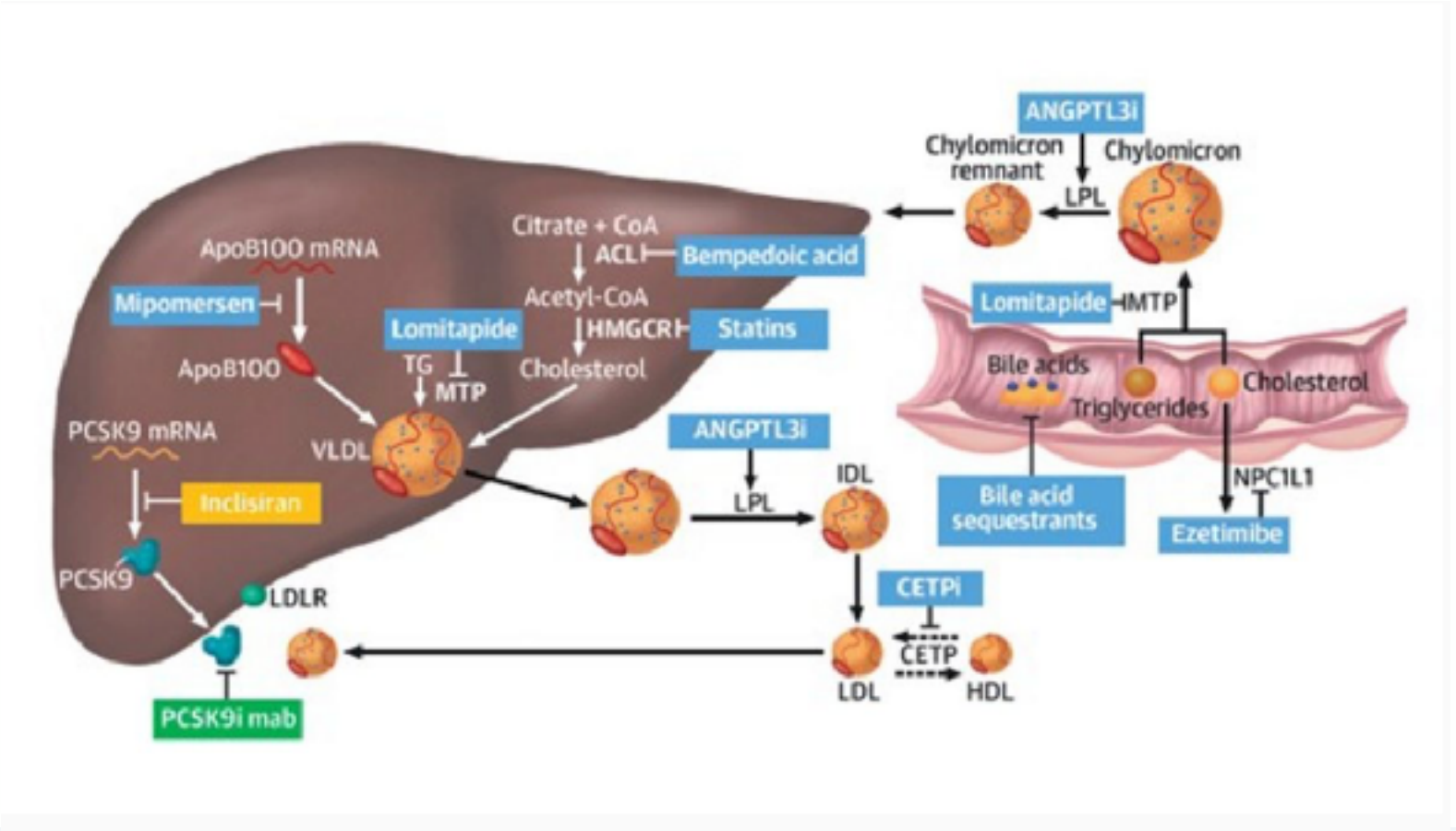
Cholesterol



Cholesterol

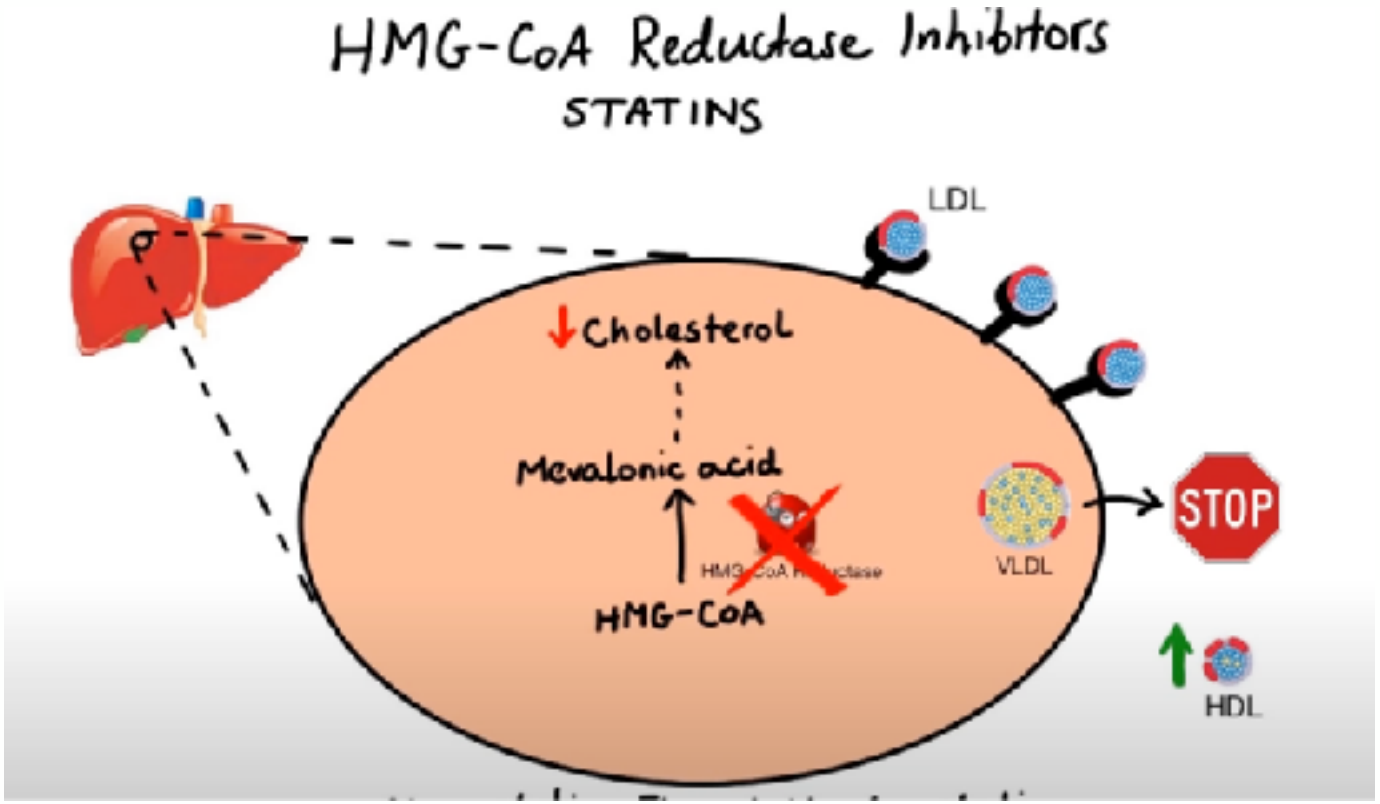
- **Causale rol van LDL-C en andere apoB bevattende lipoproteïne** bij cardiovasculaire aandoeningen (cfr. studies)
  - Verlengde daling van LDL-C -> lager risico op ASCVD
  - Relatieve reductie in CVD risico is proportioneel met de absolute LDL-daling
  - Absolute benefit of lowering LDL-C hangt af van het absolute risico op CVD en zelfs een kleine daling heeft een voordeel
- HDL-C (non high density lipoprotein): omgekeerd geassocieerd met CVD risico, hogere HDL lagere CVR
- **Lipoproteine a (Lp(a)**): verhoogd risico op CV aandoeningen, extra risicofactor, 1x tijdens het leven te bepalen

Behandeling hypercholesterolemie



Statines

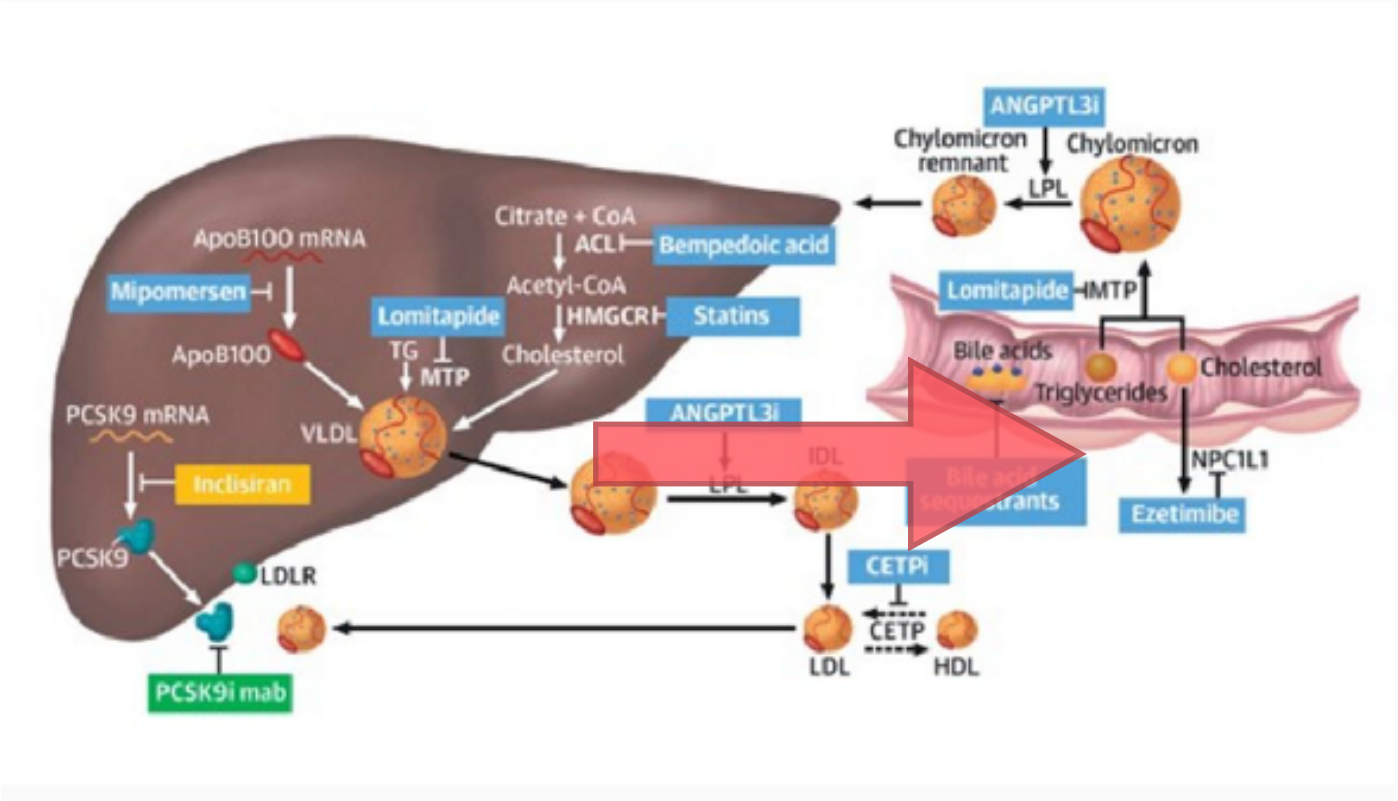
- HMG-CoA Reductase inhibitoren
- **Eerste keuze**
- Reductie van de cholesterolsynthese in de hepatocyt
- Upregulatie van de LDL-receptor
- Afname VLDL release
- Nevenwerkingen:
  - Myalgieën
  - Rhabdomyolyse (extreem zeldzaam)
  - Leverfunctiestoornissen
  -



Selectieve cholesterol absorptie inhibitoren

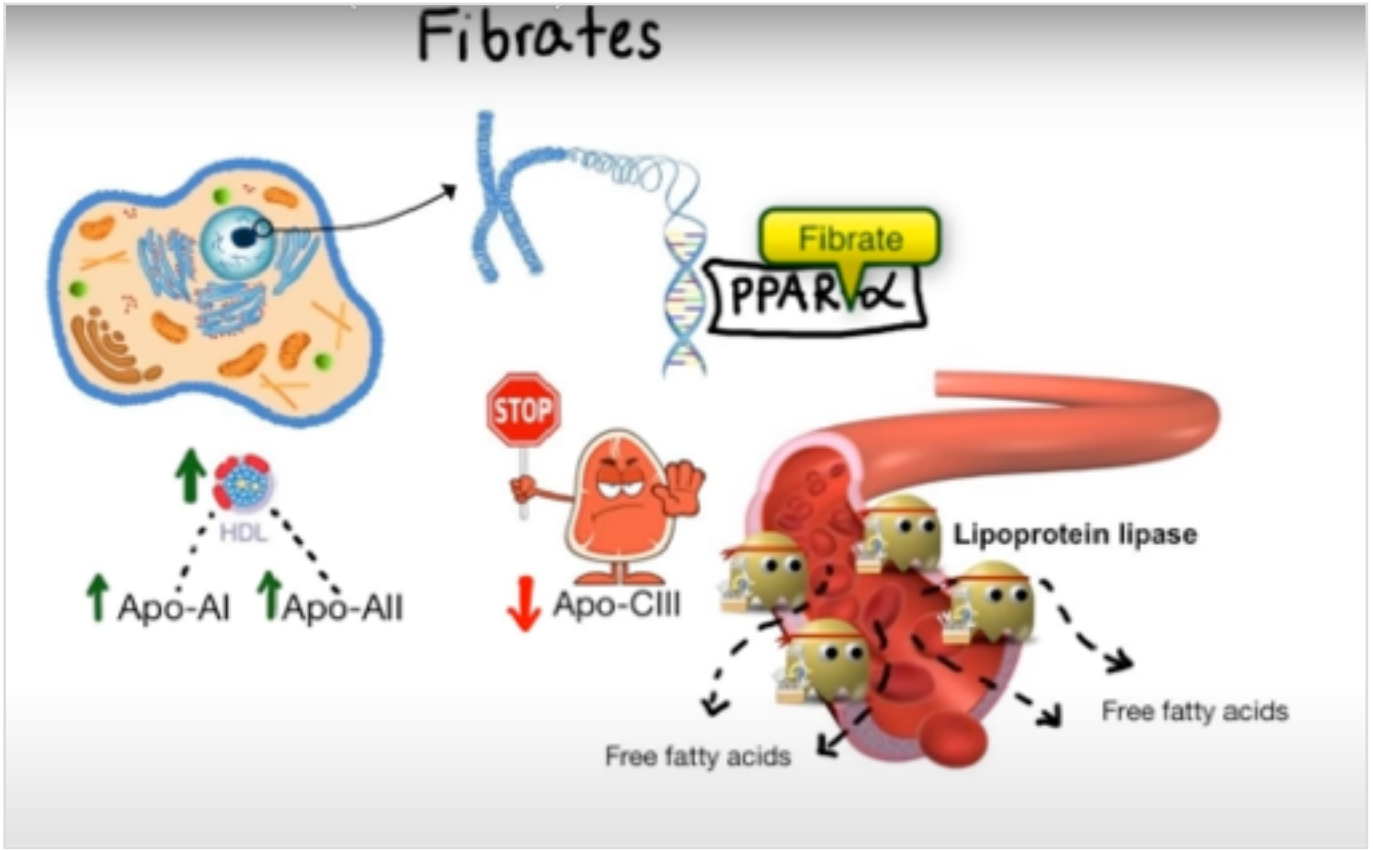
Ezetimibe

- Inhibitie van de intestinale opname van dieet en biliaire cholesterol
- Upregulatie van de LDL-R
- **Tweede keuze**



Fibraten

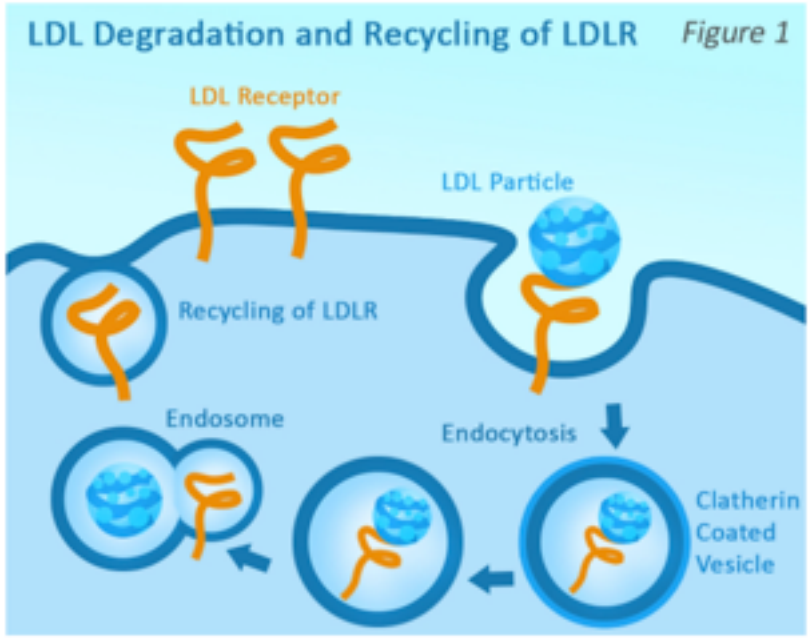
- **Eerste keuze** voor behandeling van **hypertriglyceridemie**
- **Beperkte evidentie** voor **preventie van cardiovasculaire aandoeningen**
- GI-ongemakken
- Myopathie

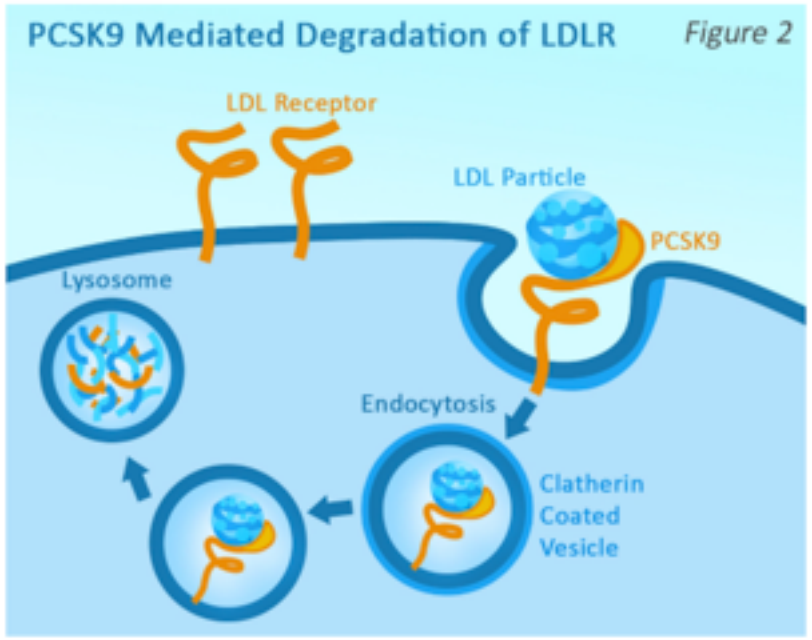


PCSK-9 inhibitoren

Monoclonale antistoffen (Alirocumab en Evolocumab)

- 2-wekelijkse/1xm toediening
- Tot 60% daling van LDL-C
- Bij voorkeur **on top off statine en Ezetimibe**
- Ook daling Lp(a) en TG en stijging HDL-C
- Cave auto-antistoffen

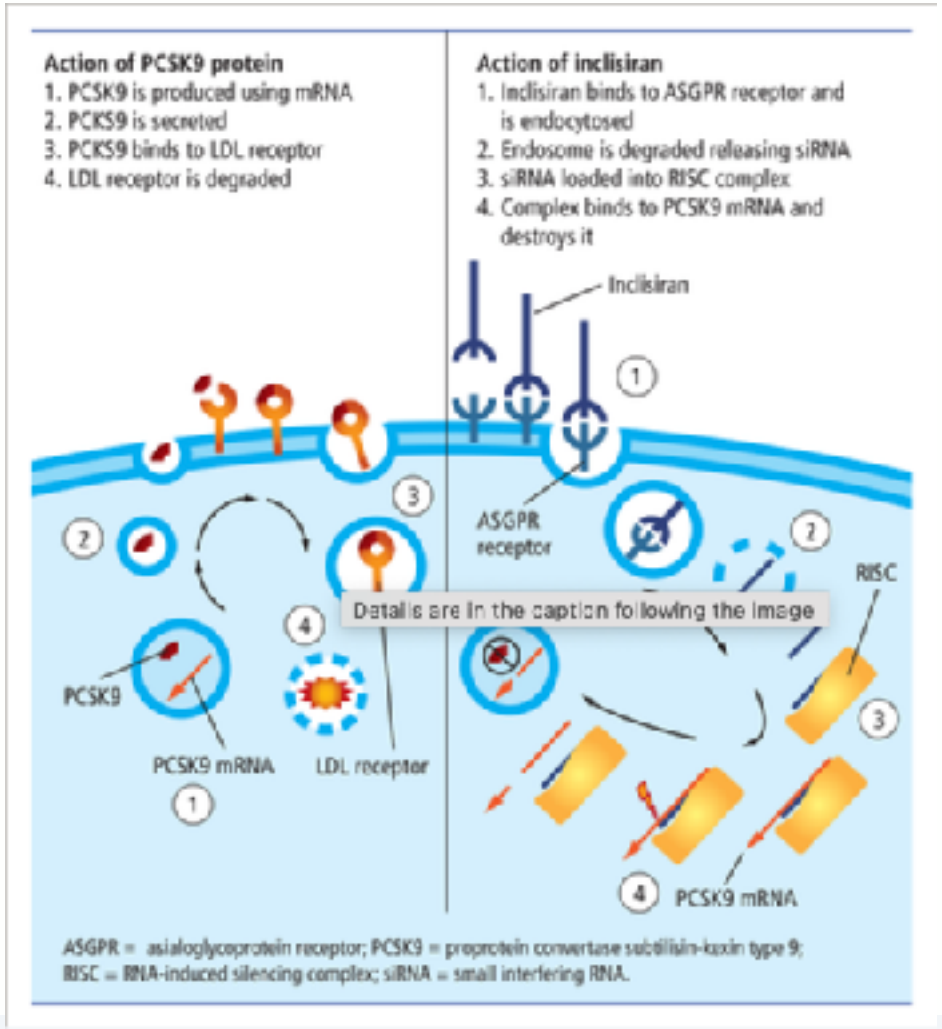




Langwerkende hepatische PCSK9 synthese inhibitor

Inclisiran (Leqvio)

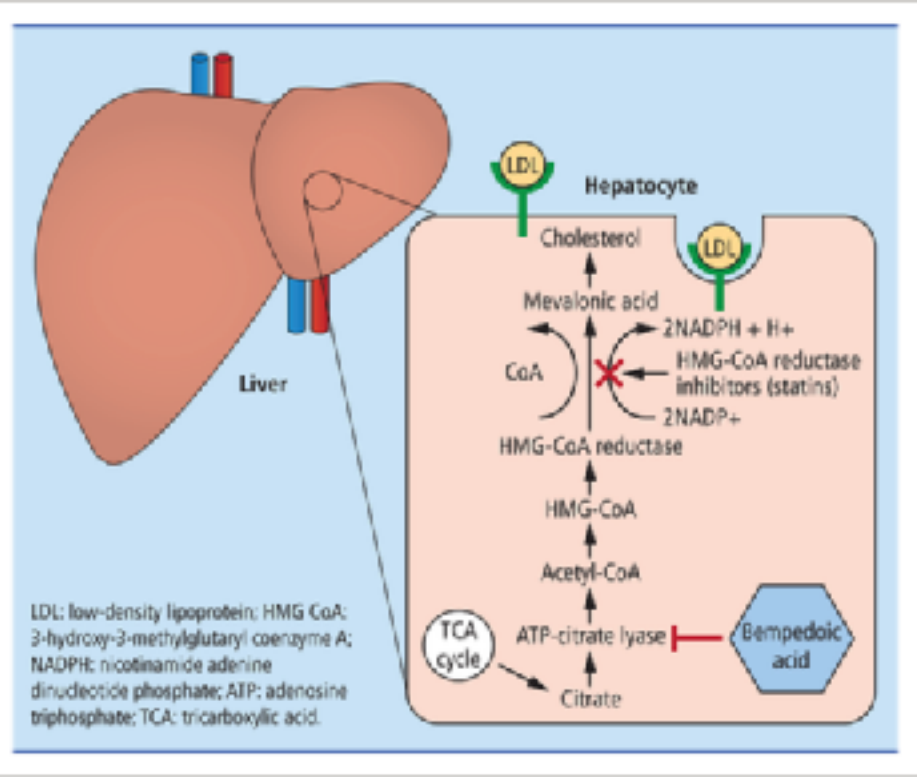
- Small interfering RNA
- Inhibeert de translatie van PCSK9
- SC toediening 2x/j
- Reductie van LDL-C van 50-55%
- Nog geen outcome trials - worden verwacht



Orale cholesterol synthese inhibitor

Bempedoïnezuur

- Vnl bij statine intolerantie
- Vaak in combinatie gebruikt met Ezetimibe
- Anemie, hyperuricemie, jicht, leverfunctiestoornissen
- cave myopathie bij gelijktijdig gebruik met statines



Wat te verwachten?

Drug class	Expected proportional LDL-C lowering compared with placebo	LDL-C lowering effect after 2 weeks of treatment[a]
Moderate-intensity statin	30%	25%[84]
High-intensity statin	50%	45%[85]
ezetimibe	20%	20%[86]
PCSK9 antibody	60%	50–60%[79,80,87,88]
PCSK9 siRNA	50%	40%[32]
Bempedoic acid	15–25%	15–25%[89]
Combination therapy		
High-intensity statin plus ezetimibe	65%	
High-intensity statin plus PCSK9 antibody	75%	
High-intensity statin plus ezetimibe plus PCSK9 antibody	85%	
Bempedoic acid plus ezetimibe	35%	

Hoe behandelen?

- Onderliggende aandoeningen uitsluiten en be
- Levensstijl!
- LDL-goal bereik
- Shared-decision
- Stapsgewijze int behandeling
  - minder neve
  - betere toler
  -

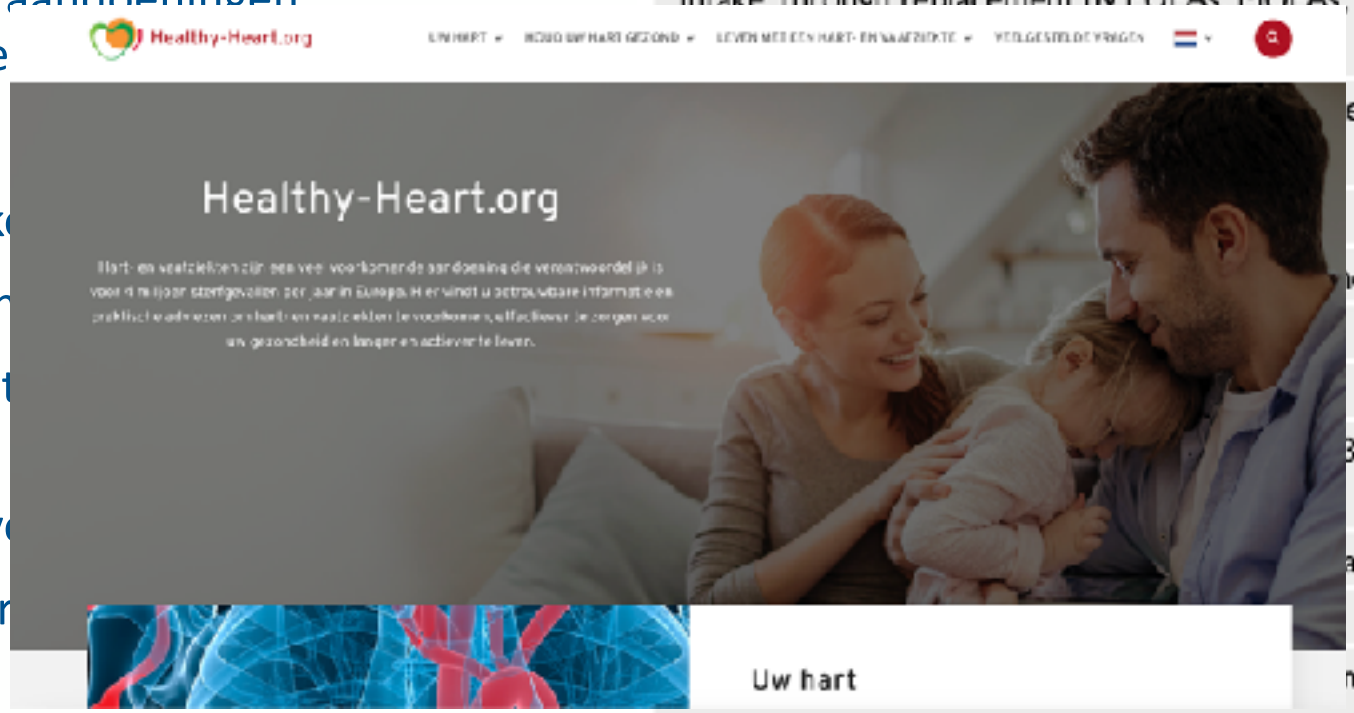


Table 8 Healthy diet characteristics

Adopt a more plant- and less animal-based food pattern
Saturated fatty acids should account for <10% of total energy intake, through replacement by PUFAs, MUFAs, and carbohydrates from
ed as far as possible, with
olegrains
350 - 500 g a week, in par-
articular fatty fish
maximum of 100 g per week
Sugar-sweetened beverages, such as soft drinks and fruit juices, must be discouraged

Wie behandelen?

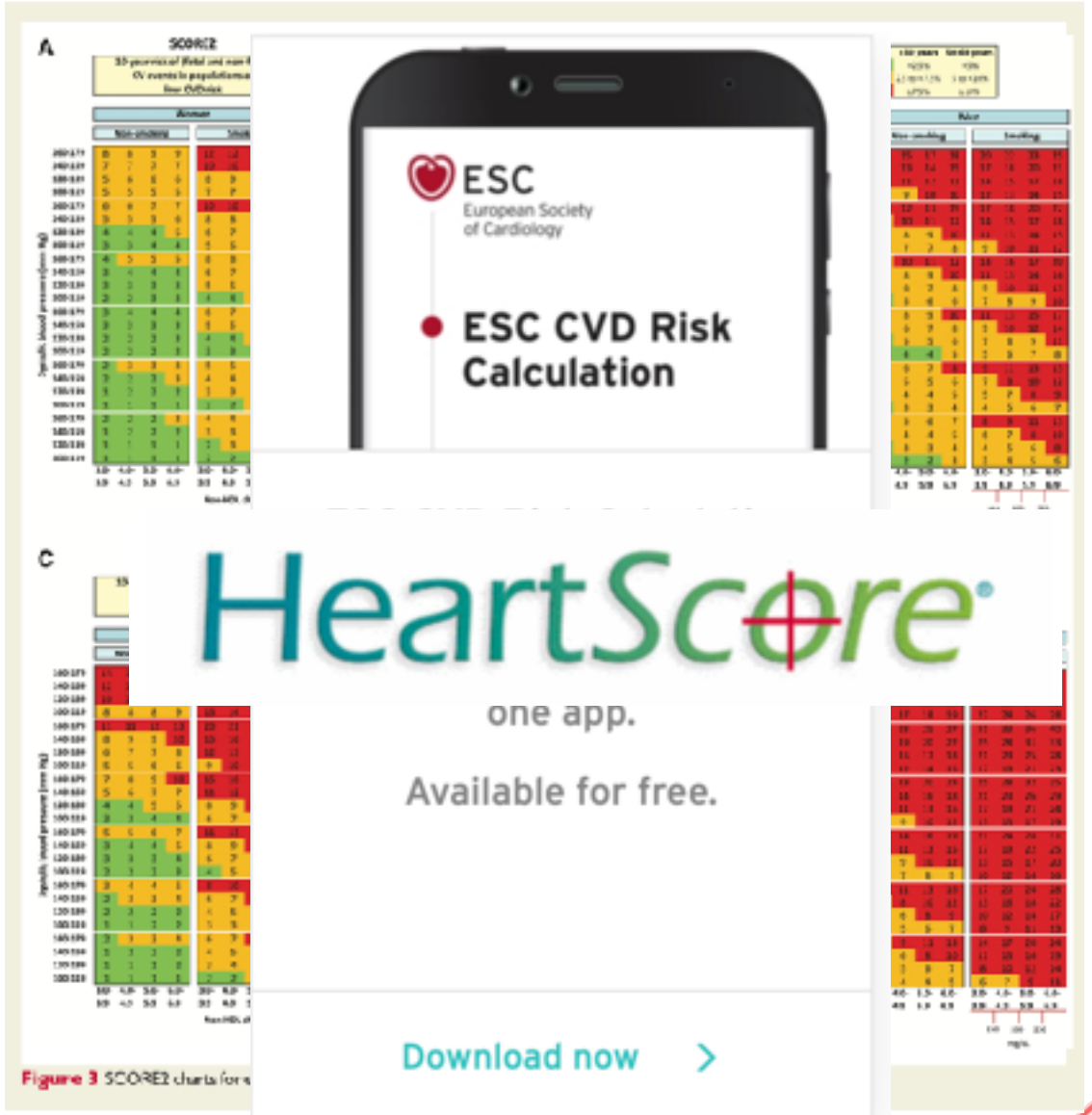
SCORE 2 en SCORE-OP

- Momentopname - elke 5 jaar herhalen
- Niet van toepassing bij:
  - CVD
  - DM
  - matig tot ernstig nierlijden
  - genetische of zeldzame lipiden of BD aandoeningen

  = Hoog of zeer hoog risico patiënten

RISICO - MODIFIERS

- Coronaire calcium score
- Lp(a)



Preventie bij ‘gezonde’ personen’

- **Personen <u>zonder:</u>**

- Diabetes mellitus

- Bevestigde atherosclerotische aandoeningen

- Chronische nierlijden

- Familiale hypercholesterolemie

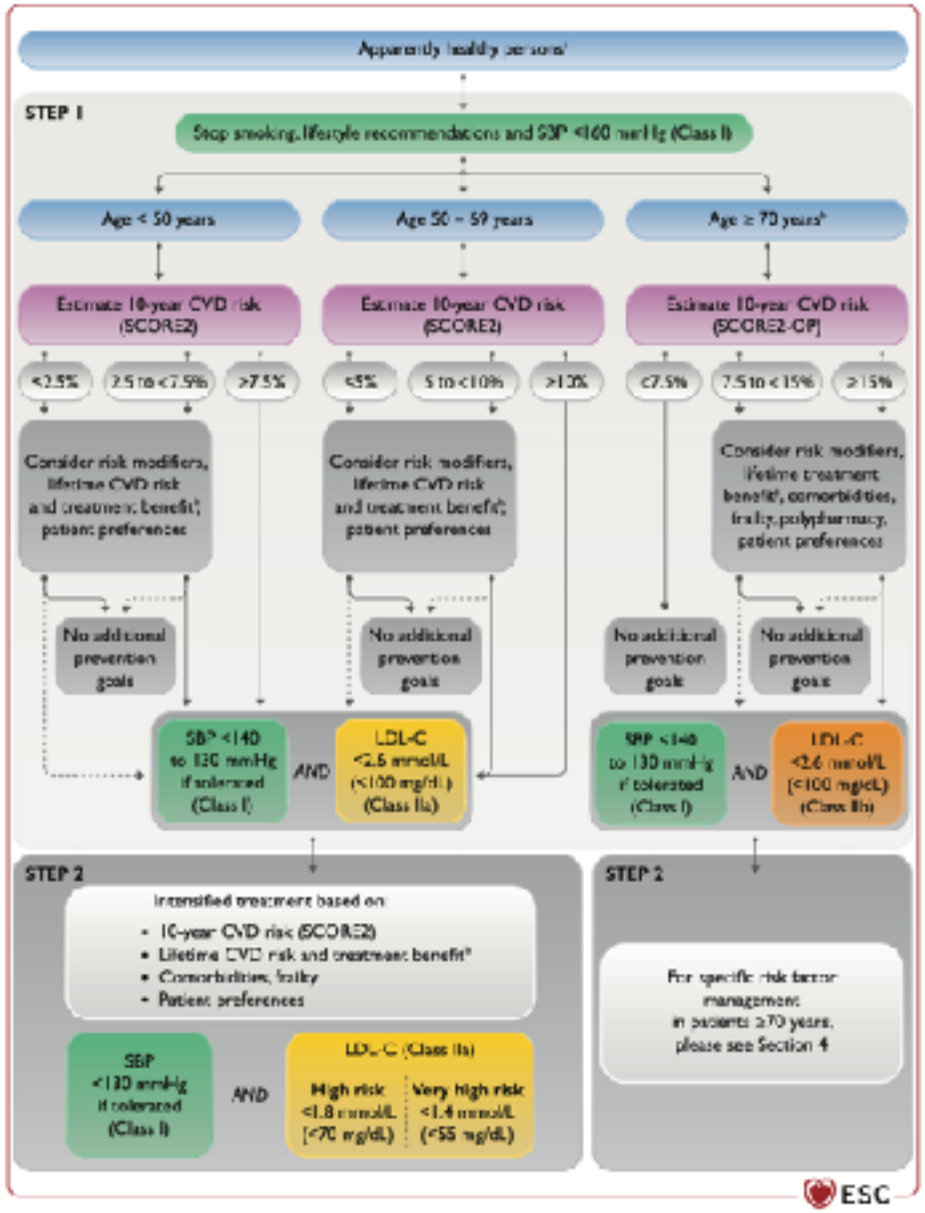
- **Shared decision making**

- **> 70 jaar:**

- Statine in primaire preventie te overwegen bij zeer hoog risico

- Cave levensverwachting, frailty

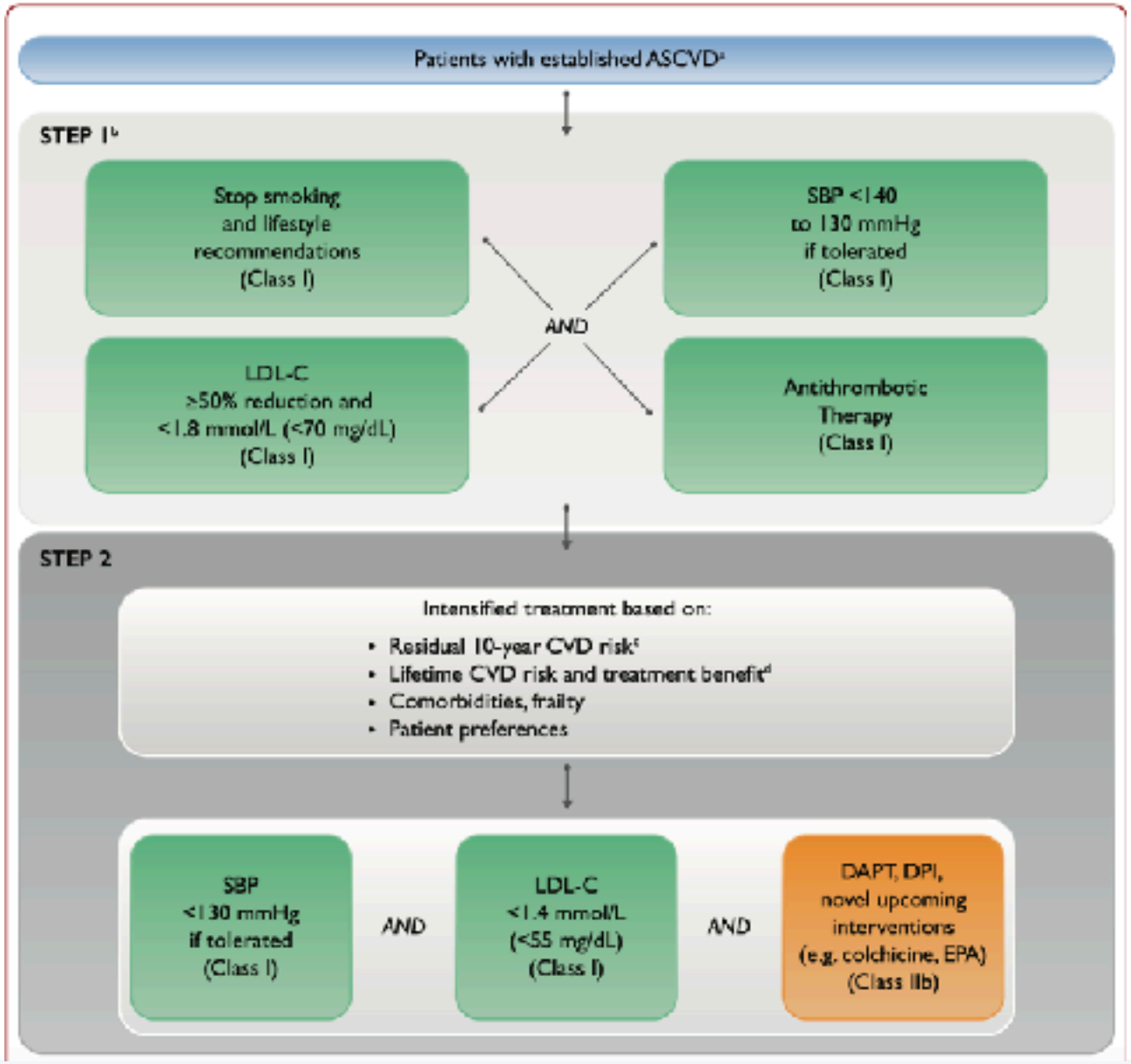
- LDL-goal <100 mg/dl



Preventie bij ‘gezonde’ personen

Samengevat

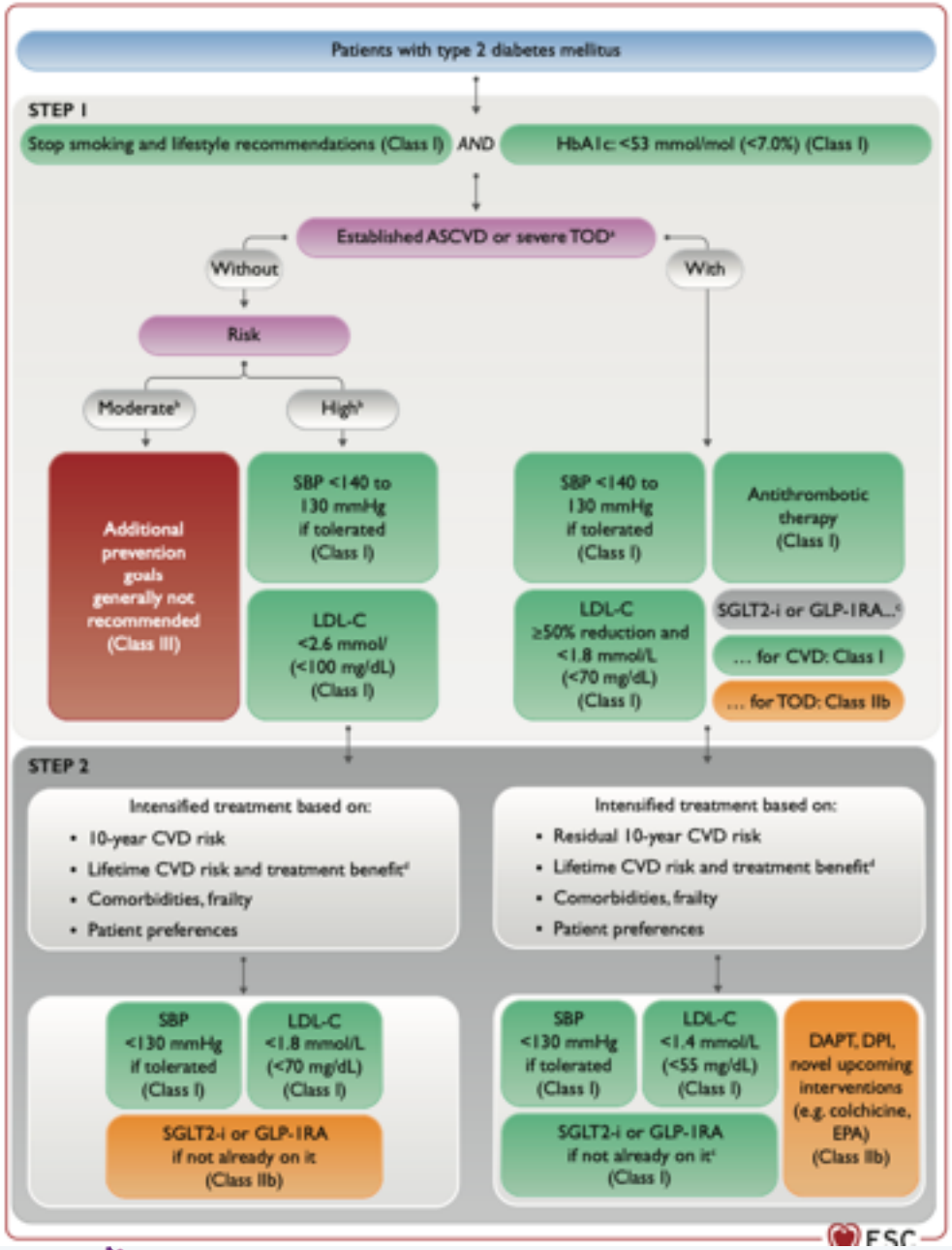
- Rookstop, levensstijlaanpassingen, SBP <160 mmHg
- Stapsgewijze aanpak
- Statine +/- Ezetimibe (+/- Bempedoïnezuur)
- Bempedoïnezuur +/- Ezetimibe


Patients with established ASCVD[a]
STEP 1[b]
Stop smoking and lifestyle recommendations (Class I)
SBP <140 to 130 mmHg if tolerated (Class I)
AND
LDL-C ≥50% reduction and <1.8 mmol/L (<70 mg/dL) (Class I)
Antithrombotic Therapy (Class I)
STEP 2
Intensified treatment based on:
• Residual 10-year CVD risk[c]
• Lifetime CVD risk and treatment benefit[d]
• Comorbidities, frailty
• Patient preferences
SBP <130 mmHg if tolerated (Class I)
AND
LDL-C <1.4 mmol/L (<55 mg/dL) (Class I)
AND
DAPT, DPI, novel upcoming interventions (e.g. colchicine, EPA) (Class IIb)

Preventie bij bewezen ASCVD

Recommendations for pharmacological LDL cholesterol lowering

Recommendations	Class	Level
In patients with established ASCVD, lipid-lowering treatment with an ultimate LDL-C goal of ≥50% reduction vs baseline and an LDL-C of <1.4 mmol/L (<55 mg/dL) is recommended.	I	A
If the goals are not achieved with the maximum tolerated dose of a statin, combination with ezetimibe is recommended.	I	B
For secondary prevention patients not achieving their goals on a maximum tolerated dose of a statin and ezetimibe, combination therapy including a PCSK9 inhibitor is recommended.	I	A


Patients with type 2 diabetes mellitus
STEP 1
Stop smoking and lifestyle recommendations (Class I)
AND
HbA1c: <53 mmol/mol (<7.0%) (Class I)
Established ASCVD or severe TOD[a]
Without
With
Risk
Moderate[b]
High[b]
Additional prevention goals generally not recommended (Class III)
SBP <140 to 130 mmHg if tolerated (Class I)
LDL-C <2.6 mmol/ (<100 mg/dL) (Class I)
SBP <140 to 130 mmHg if tolerated (Class I)
LDL-C ≥50% reduction and <1.8 mmol/L (<70 mg/dL) (Class I)
Antithrombotic therapy (Class I)
SGLT2-i or GLP-1RA...[c]
... for CVD: Class I
... for TOD: Class IIb
STEP 2
Intensified treatment based on:
• 10-year CVD risk
• Lifetime CVD risk and treatment benefit[d]
• Comorbidities, frailty
• Patient preferences
Intensified treatment based on:
• Residual 10-year CVD risk
• Lifetime CVD risk and treatment benefit[d]
• Comorbidities, frailty
• Patient preferences
SBP <130 mmHg if tolerated (Class I)
LDL-C <1.8 mmol/L (<70 mg/dL) (Class I)
SGLT2-i or GLP-1RA if not already on it (Class IIb)
SBP <130 mmHg if tolerated (Class I)
LDL-C <1.4 mmol/L (<55 mg/dL) (Class I)
SGLT2-i or GLP-1RA if not already on it[c] (Class I)
DAPT, DPI, novel upcoming interventions (e.g. colchicine, EPA) (Class IIb)
ESC

Familiale hypercholesterolemie

- HeFH incidentie 1/200-250
- Denk eraan bij LDL-C >190 mg/dl
- Screening 1e graadsverwanten
- Hoogrisico ptn: LDL-C<70 mg/dl
- +1 RF: LDL-C <55 mg/dl
- Therapie
  - Statine + Ezetimibe + Bempedoïnezuur
  - PCSK-9 inhibitor
  - Inclisiran

Table 11 Dutch Lipid Clinic Network diagnostic criteria for familial hypercholesterolaemia

Criteria (choose only one score per group, the highest applicable; diagnosis is based on the total number of points obtained)	Points
1) Family history	
First-degree relative with known premature (men aged <55 years; women <60 years) coronary or vascular disease, or first-degree relative with known LDL-C above the 95th percentile	1
First-degree relative with tendinous xanthomata and/or arcus corneals, or children aged <18 years with LDL-C above the 95th percentile	2
2) Clinical history	
Patient with premature (men aged <55 years; women <60 years) CAD	2
Patient with premature (men aged <55 years; women <60 years) cerebral or peripheral vascular disease	1
3) Physical examination	
Tendinous xanthomata	6
Arcus corneals before age 45 years	4
4) LDL-C levels (without treatment)	
LDL-C ≥8.5 mmol/L (326 mg/dL)	8
LDL-C 6.5–8.4 mmol/L (251–325 mg/dL)	5
LDL-C 5.0–6.4 mmol/L (191–250 mg/dL)	3
LDL-C 4.0–4.9 mmol/L (155–190 mg/dL)	1
5) DNA analysis	
Functional mutation in the LDLR, apolipoprotein B, or PCSK9 genes	8
A 'definite' FH diagnosis requires >8 points	
A 'probable' FH diagnosis requires 6–8 points	
A 'possible' FH diagnosis requires 3–5 points	

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